

Synthesis some of heterocyclic compounds derived from thymol

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الخلاصة

في هذا البحث حضرت بعض مركبات الهيدرازون (3-7) من خلال مفاعلة الهيدرازيد (2) مع معوضات البنزالديهايد. أما مشتقات الاوكسازيريدين (8-12) تم تحضيرها عن طريق أكسدة الهيدروزونات (3-7) بواسطة حامض الميتا كلورو بنزويك الفوقي. عند مفاعلة المركبات الناتجة (8-12) مع ثايوسيانات المونيا أعطت مشتقات الثايازولدين (13-17). وعند مفاعلة المركب (2) مع الاندول -3,2 ثنائي أون اعطت المركب (18) والذي عند تفاعله مع الثايو حامض الخليك اعطى مشتق السبايرواندولين -3,2-ثايازولدين (19) والذي عند مفاعله مع حامض الكبريتيك المركز أعطى المركب (20) في حين مفاعلة المركب (19) مع خماسي كبريتيت ثنائي الفوسفور اعطى المركب (21).

Abstract

A series of some hydrazones derivatives (3-7) have been synthesized from the reaction of hydrazide (2) with substituted benzaldehyde. While oxaziridine derivatives (8-12) were synthesized by oxidation with hydrazones derivatives (3-7) with m-chloro per benzoic acid, the of these compounds (8-12) with ammonium thiocyanate afforded compounds (13-17). While the reaction of compound (2) with indole-2,3-dione afforded compound (18) while in reaction with mercaptoacetic acid gave Spiro indoline-2,3-thizolidine derivatives (19) when the compound allowed to react with conc., sulfuric acid and phosphoric pent oxide afford (20) and (21) respectively.

Introduction

Hydrazones derivatives have aroused considerable interest due to the used as intermediate to synthesis several heterocyclic compounds^[1]. Oxaziridine compounds synthesized from oxidation of imines derivatives using m-chloroperbenzoic acid^[2] or through oxidation of hydrazones by per benzoic acid^[3]. literature survey reveals that indole and thiazolidinone Derivatives are important for anti-inflammatory^[4,5], analgscic^[6],

antibacterial^[7] activities. Also several oxadiazol and thidazol derivatives have been found to be of interest with potential activities including antiinflammatory^[8] insecticidal activities^[9].

Experimental

Melting points were measured on Electro thermal Melting Point Apparatus and are uncorrected. The IR spectra were recorded by using infrared spectrophotometer model Tensor 27 Brucker Co. Germany.

Ethyl thymoxy acetate^[1]

This compound was prepared from the reaction of (0.06 mole, 9.0g) thymol, (0.06 mol, 8.28g) anhydrous potassium carbonate and (0.06 mole, 10.14g) bromoethylacetate following the method describe in the literature^[10], gave 96%, colorless oily product.

Thymoxy acetic acid hydrazide^[2]

This compound was prepared from the reaction of (0.05 mole, 12.89g) ester (1) and (0.25mole, 12.5g) hydrazine hydrate 99% as mentioned in the literature^[10], yield 87%, m.p.(93-95 °C), lit.(93-95 °C).

Hydrazones^[11] (3-7)

A mixture of hydrazide (2) (0.01 mole, 2.22g) and substituted aromatic aldehyde (0.01 mole) in 25ml ethanol, was heated under refluxed for 2 hours. After completion of reaction, it was cooled to room temperature. The precipitate was filtered and recrystallized from ethanol, to give the hydrazones (3-7). Some physical and spectral data indicated in Table (1, 4).

Thymoxy methyl acetamido-2-aryl oxaziridine^[12] (8-12)

Hydrazones derivatives (3-7) (0.001mole) was dissolve in dry pyridine (4-6ml), followed by adding m-chloro per benzoic acid (0.002 mole, 0.34 g) (dissolved in 5 ml pyridine). The mixture was stirred for (12hours) at room temperature, ice-water was added and lefted over night, the precipitate was filtered and washed with hot water, dried. Recrystallization from ethanol afforded the required compounds (8-12). Some physical and spectral data indicated in Table (2, 5).

2-Thymoxy methyl acetamido-2-aryl thiazirdine^[13] (13-17)

Stirred a mixture of the appropriate oxazirdine derivative (8-12) (0.001 mol) in (15ml) dimethylforamide, ammonium thiocyant (0.002mole, 0.15g) (dissolved in 5ml DMF) was then added drops wise. The reaction mixture was stirred at room temperature for further 24 hrs, ice crushed ice was added to the reaction mixture and left for 4hrs, the

precipitate was filtered and recrystallized from ethanol. The physical properties and spectral data were indicated in Table (3, 6).

2-(2-isopropyl-5-methyl phenoxy)-N-[2-oxo-1, 2-dihydro-3H-indol-3-ylidene] acetylhydrazide ^[14] (18)

A mixture of (0.01 mol, 2.22g) (2) and indole-2,3-dione (1.47g, 0.01mol) in methanol (60ml) in the presence of catalytic amount of glacial acetic acid was heated under refluxed for 1hr. The solid separated on cooling was filtered, washed with cold methanol and recrystallized from methanol to give yellow crystals product, m.p. (230-232°C), and 88%.

2-(2-isopropyl-5-methyl)phenoxy-N-(2,4-dioxospiro[indolin-3,2-thiazolidin)-3-yl] acetamide ^[14, 15] (19)

A mixture of (0.001mol, 0.35g) (19) and mercapto acetic acid (0.002mol, 0.18g) in DMF (50ml) in presence of anhydrous ZnCl₂ was heated under refluxed for 6-8hrs, the precipitate was filtered and recrystallized from dimethyl sulfoxide to afford yellowish product, m.p.(197-199°C), 53%.

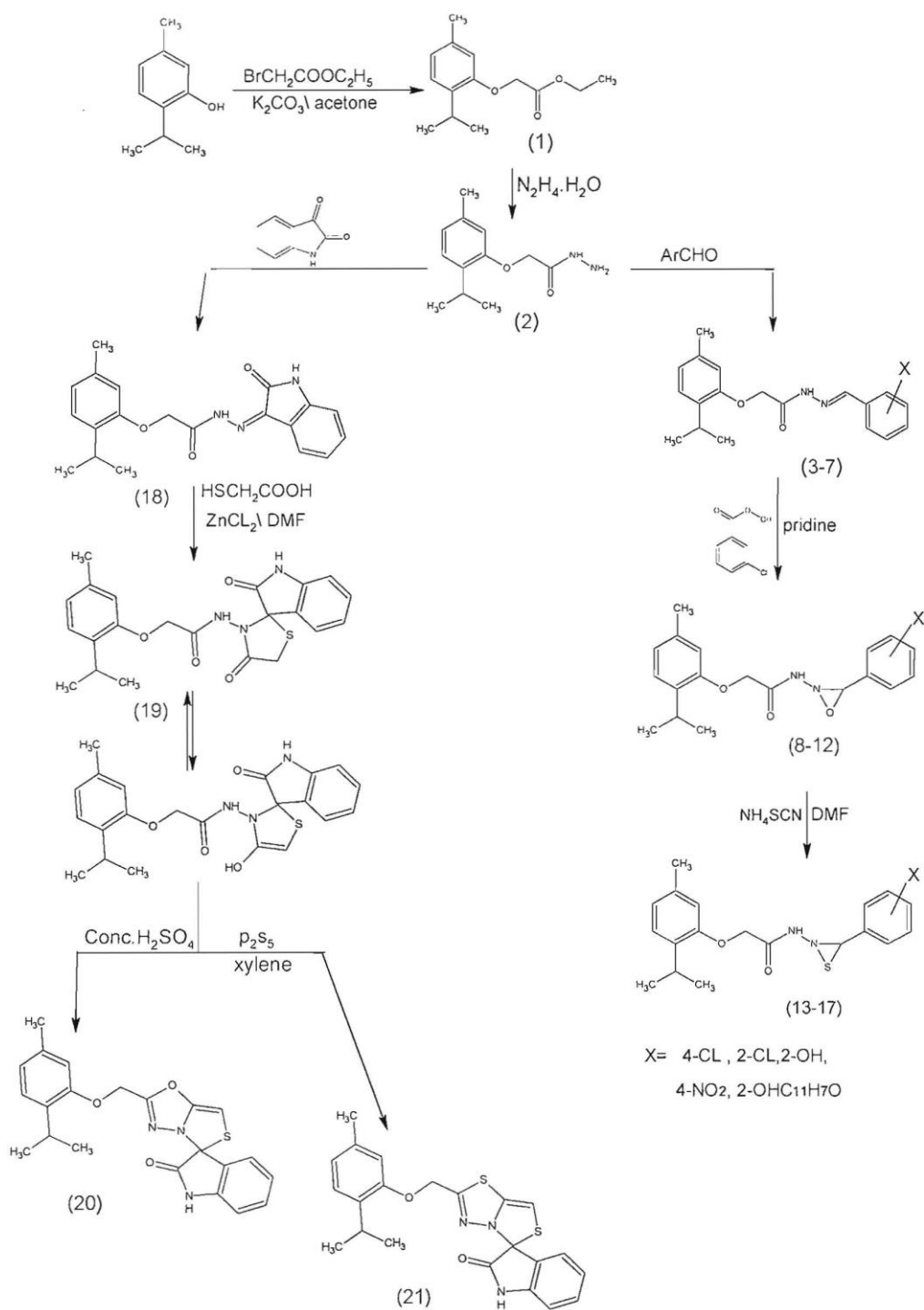
2-(2-isopropyl-5-methyl) phenoxy methyl Spiro [indolin-3, 5-thiazolo[4,3-b] [1, 3, 4] oxadiazol]-2-one ^[14](20)

To compound (19) (0.11 g), Conc. sulfuric acid (3ml) was added drop wise under cooling, The mixture was kept for (6hrs) at room temperature, after that crush ice was added, the mixture was neutralized with ammonium solution, the precipitate was filtered, wash with water and recrystallized from DMF to afford pale brown product, m.p(120-122°C), 30% .

2-(2-isopropyl-5-methyl) phenoxy methyl Spiro [indolin-3, 5-thiazolo [4,3-b] [1,3, 4-thiazol]-2-one (21)

A mixture of (0.00047mol, 0.020g) (19) and P₂S₅ (0.0023 mol, 0.50g) in xylene (15ml) was heated under refluxed for 5 hrs. Then the mixture was filtered while hot, after cooling and evaporation of the solvent. The precipitate was washed with ether to afford green-yellow product, m.p. (215-217 °C) and 49%.

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Scheme (1): general scheme for reactions

Results and Discussion

The hydrazones derivatives (3-6) were obtained from refluxing Hydrazide (2) with substituted benzaldehyde in ethanol. The compounds were identified by IR which exhibits characteristic bands in the following range. The bands at (3196-3444 cm^{-1}) were assigned for the (N-H) group. While the bands at (1677-1688 cm^{-1}) related to the carbonyl group. While the bands within the range (1604-1637 cm^{-1}) related to the (C=N) group. The IR spectra were shown in Table (1).

Oxaziridine derivatives (8-12) were prepared by the reaction of appropriate hydrazones derivatives with m-chloroperbenzoic acid in pyridine. The structure was elucidated using spectral data. The infrared spectra Table(2) showed absorption bands at (3194-3320 cm^{-1}) for the (N-H) group, also bands at (1677-1694 cm^{-1}) due to (C=O) groups, also bands at (1601-1639 cm^{-1}) for aromatic (C=C) group. The stretching absorption bands for (N-O) and (C-O) groups appeared at (669-785 cm^{-1}), and (1076-1306 cm^{-1}).

The reaction of appropriate oxaziridine (8-12) with ammonium thiocyanate afforded thiaziridine (13-17) which were identified by IR as shown in Table (3). The appearance of bands at (1678-1698 cm^{-1}) for the carbonyl stretching vibration, while bands at (1604-1624 cm^{-1}) are due to aromatic (C=C) stretching. The spectrum also showed bands at (600-721 cm^{-1}) for (C-S), while (N-H) stretching vibration was absorbed at (3197-3444 cm^{-1}), chemical tube identification gave positive test for sulfur.

The condensation of hydrazide compound (2) with indole-2,3-dione in methanol in presence of a few drops of glacial acetic acid afforded compound (18) which was identified by the appearance of the following bands at (1715 cm^{-1}) related to the carbonyl of lactam group of indole and the band absorbed at (1624 cm^{-1}) attributed to the stretching vibration of aromatic (C=C) group, while the band at (1604 cm^{-1}) attributed to (C=N) group. Also the spectrum shows band at (3209 cm^{-1}) due to (N-H) stretching vibration.

The reaction of compound (18) with thioglycolic acid in dimethyl formamide in presence of zinc chloride afforded compound (19), the product was identified by the stretching bands at (1715 cm^{-1}) for lactam which appeared at lower value than expected region due to enol-keto tautomerism, while bands at (1686 cm^{-1}) assigned to amidic groups. Also a band at (1604 cm^{-1}) was attributed to the stretching vibration of (C=N) group. Band at (719 cm^{-1}) assigned to (C-S-C) bond. The spectrum also showed bands at (3213 cm^{-1}) which was for (N-H) stretching.

On the other hand a new band for vibration for (O-H) group appeared at (3405 cm^{-1}), while a band at (1338 cm^{-1}) was assigned for (C-N) stretching vibration.

The reaction of compound (18) with conc. H_2SO_4 gave compound (20). This compound was identified by IR spectrum which showed the appearance of the following bands at (1717 cm^{-1}) for stretching band of carbonyl group of indole, band at (1615 cm^{-1}) for stretching vibration of (C=N) group and bands at (1085 and 1243 cm^{-1}) for symmetrical and unsymmetrical stretching vibration of (C-O-C) group, other band appeared at (1620 cm^{-1}) for the stretching (C=C) group and band at (3202 cm^{-1}) for stretching vibration of (N-H) group. The spectrum also showed the disappearance of the following stretching banding of amidic carbonyl group.

The structure of compound (21), was elucidated depending on the spectral data, The spectrum, showed the following absorption bands at (1716 cm^{-1}) for indole carbonyl stretching, also the IR spectrum identified by the disappearance of amidic carbonyl bands and thiazoliden carbonyl group. The appearance of bands at (1687 and 1626 cm^{-1}) was assigned to (C=N) and aromatic (C=C) bond respectively. Two absorption bands at (750 and 787 cm^{-1}) were related to symmetrical and asymmetrical (C-S-C) group respectively. In addition, the stretching at (3211 cm^{-1}) is assigned for (N-H).

Table(1):physical data for hydrazones derivatives(3-7)

Comp. No.	X	m.p($^{\circ}\text{C}$)	Yield(%)	Color
3	4-CL	165-167	79	White
4	2-CL	152-154	75	Yellowish-white
5	2-OH	140-142	81	White
6	4-NO ₂	136-138	77	Pall-yellow
7	2-OHC ₁₁ H ₇ O	182	83	Green-yellow

Table(2):physical data for oxaziridine derivatives(8-12)

Comp. No.	X	m.p($^{\circ}\text{C}$)	Yield(%)	Color
8	4-CL	172-174	91	White
9	2-CL	178-180	65	White
10	2-OH	163-165	72	White
11	4-NO ₂	150	75	White
12	2-OHC ₁₁ H ₇ O	177-178	89	Green

Table(3):physical data for thiaziridine derivatives(13-17)

Comp. No.	X	m.p(°C)	Yield(%)	Color
13	4-CL	169-170	73	White
14	2-CL	182-183	77	Pale brown
15	2-OH	167-168	83	White
16	4-NO ₂	125-126	85	Pale yellow
17	2-HOC ₁₁ H ₇ O	157-159	70	Pale green

Table(4):IR spectral data for hydrazones derivatives

Comp. No.	X	IR.vCm ⁻¹ (KBr)				
		N-H	C=O	Ar C=C	C=N	Others
3	4-CL	3444	1685	1607	1613	726(C-CL)
4	2-CL	3196	1688	1601	1604	758(C-CL)
5	2-OH	3199	1677	1572	1620	3091(OH)
6	4-NO ₂	3197	1678	1614	1613	1284Sy.(NO ₂) 1506Asy.(NO ₂)
7	2-HOC ₁₁ H ₇ O	3232	1678	1678	1637	3411(OH)

Table(5):IR spectral data for oxaziridine derivatives(8-12)

Comp. No.	X	IR.vCm ⁻¹ (KBr)					
		N-H	C=O	Ar C=C	N-O	C-O	Others
8	4-CL	3320	1677	1607	785	1306	(C-CL)
9	2-CL	3203	1694	1601	749	1242	(C-CL)
10	2-OH	3200	1677	1620	752	1241	(OH)
11	4-NO ₂	3194	1689	1614	715	1254	1284Sy.(NO ₂) 1506As.(NO ₂)
12	2-HOC ₁₁ H ₇ O	3236	1680	1639	669	1076	3411(OH)

Table(6): IR spectral data for thiaziridine derivatives (13-17)

Comp. No.	X	IR.vCm ⁻¹ (KBr)				
		N-H	C=O	Ar C=C	C-S	Others
13	4-CL	3444	1678	1612	667	C-CL(727)
14	2-CL	3197	1688	1604	600	C-CL(758)
15	2-OH	3218	1698	1604	676	O-H(3446)
16	4-NO ₂	3197	1687	1614	690	Sy.NO ₂ (1265) Asy.NO ₂ (1522)
17	2-HOC ₁₁ H ₇ O	3236	1682	1624	721	O-H(3413)

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